ASX ANNOUNCEMENT

Actinogen December 2023 quarterly activity report and Appendix 4C

Sydney, 30 January 2024. Actinogen Medical ASX: ACW ("ACW" or "the Company") is pleased to announce the release of its quarterly activity report and Appendix 4C for the three-month period ended 31 December 2023.

- **$4.8 million R&D tax incentive rebate received**
    - The Company announced on 28 November that it had received a research and development (R&D) tax incentive rebate of $4.8 million from the Australian Tax Office for the 2023 financial year
    - The R&D tax incentive is an Australian federal government program under which companies receive cash refunds for eligible research and development expenditure.
- **XanaCIDD Phase 2a clinical trial progress:**
    - Enrolment of patients with cognitive impairment associated with persistent major depressive disorder (MDD) continues in the XanaCIDD Phase 2a trial. Treatment with the study drug, Xanamem® or placebo is for six weeks
    - The full complement of clinical sites is open in Australia and the UK and are actively recruiting, enrolling and treating patients, with enrolment now at approximately 70% (108 of 160 planned participants)
    - Results are still anticipated in Q2 CY2024.
- **XanaMIA Phase 2b clinical trial progress:**
    - The first Australian investigational sites have been activated for the XanaMIA Phase 2b clinical trial of Xanamem enrolling 220 patients with mild to moderate Alzheimer's disease (AD)
    - Sites have begun to recruit patients for screening with an elevated blood pTau biomarker (the same biomarker used to select patients shown to have a large Xanamem clinical benefit in the previous Phase 2a biomarker trial)
    - Treatment will be with either 10mg Xanamem or placebo daily over 36 weeks
    - Enrolment of the first 100 patients will take place at Australian sites, and an administrative interim analysis will occur when approximately 100 patients reach 24 weeks of treatment (interim results expected H1 CY2025).
    - Final results are anticipated in H2 CY2025.

® Xanamem is a registered trademark of Actinogen Medical Limited

- **Manufacturing:**
    - The Company's new contract manufacturer, Asymchem, has completed the development of an improved synthetic process of Xanamem drug substance and completed the manufacture of a 1kg demonstration batch as a prelude to larger scale manufacture.
- **Executive team:**
    - In November, the Company announced the appointment of Mr Will Souter as full time Chief Financial Officer, commencing next Monday, 5 February 2024
    - Mr Souter will lead the finance, investor communications, legal and human resources functions, allowing CEO Steven Gourlay to focus on maturing business development relationships and delivering high quality trial outcomes from the current Phase 2 trials.
- **CEO and CMO presented at key international conferences and industry meetings, including:**
    - The BIO Investor Forum in San Francisco, USA on 18 October, where CEO Dr Steven Gourlay conducted investor and industry meetings
    - The 16th annual CTAD conference in Boston, USA on 25 October where CMO Dr Dana Hilt presented an academic poster that provided an overview of the Xanamem therapeutic rationale, the positive results of two prior placebo-controlled trials in healthy volunteers demonstrating pro-cognitive effects, and a biomarker trial in patients with mild Alzheimer's disease that showed cognitive and clinical benefit. CEO Dr Steven Gourlay also attended the conference and was joined by Dr Hilt in key external meetings with other Biotech/Pharma companies and investors
    - The Sachs Associates 7th Annual Neuroscience Innovation Forum in San Francisco, USA on 7 January where CMO Dr Dana Hilt recapped the strong scientific rationale for modification of brain tissue cortisol levels with Xanamem, presented the clinical benefits seen in multiple trials to date and outlined the design of the two on-going Phase 2 trials, with near-term major results in Depression and Alzheimer's disease in 2024 and 2025 respectively
    - Immediately following the Sachs Forum, CEO Dr Steven Gourlay and CMO Dr Hilt participated in a significant number of partnering, analyst and investor meetings associated with the 42nd Annual J.P. Morgan Healthcare Conference from 8 to 12 January.
- **Cash balance of $11.5 million at 31 December 2023.**[1]
- **Xanamem human brain PET[2] study published in peer-reviewed journal *The Journal of Alzheimer's Disease***

  On 19 January 2024 this study was published and can be accessed by the following link: https://pubmed.ncbi.nlm.nih.gov/38250767/

  The study concluded that:

  1) Xanamem achieved high target occupancy of 66-85%, which exceeded the 30-60% inhibition required for effectiveness in animal models
  2) A dose level of 10 mg daily achieved near saturation of the enzyme target, meaning that higher doses achieved little additional occupancy
  3) The study results support exploring doses of ≤10 mg in clinical trials, consistent with the Company's ongoing phase 2 trials.

[1] Unless stated otherwise, all financial data is in Australian dollars
[2] Positron Emission Tomography

Dr Steven Gourlay, Actinogen's CEO and MD, said:

"The Company continues to make very good progress in enrolling participants in our XanaCIDD Phase 2a trial in patients with cognitive impairment associated with persistent MDD. Enrolment now approximates 70% and trial results are expected in Q2 2024, which is only a few months away. We were also delighted to activate the first investigational site in our XanaMIA Phase 2b Alzheimer's disease trial prior to the December holiday break.

"Actinogen also continues to be a major beneficiary of the Australian government's R&D tax incentive scheme, with a tax refund of $4.8 million received last year contributing significantly to our clinical trial funding. With a focus on Australian clinical trial operations in the current financial year, we expect the next R&D tax incentive rebate in H2 CY2024 to be larger again."

Cash position

Actinogen's cash balance at 31 December 2023 was $11.45 million.

Net operating cash outflow for the quarter was $1.63 million, including R&D spend of $4.97 million and staff costs of $0.89 million.

The increase in R&D spend for the December quarter ($4.97 million) compared to the September quarter ($3.23 million) reflected increased clinical trial activity as the XanaMIA Phase 2b AD trial commenced investigational site activation.

The Company received an R&D tax incentive refund from the Australian Tax Office for the 2023 financial year of approximately $4.79 million on 28 November 2023.

Consistent with ASX Listing Rule 4.7c.3, item 6 of the attached Appendix 4C of the cashflow report for the quarter included payments to Related Parties of $0.20 million, comprising the salary and bonus for the CEO/Managing Director, fees paid to Non-Executive Directors and superannuation.

ENDS

Investors

Dr. Steven Gourlay
CEO & Managing Director
P: +61 2 8964 7401
E. steven.gourlay@actinogen.com.au

Michael Roberts
Investor Relations
M: +61 423 866 231
E. michael.roberts@actinogen.com.au

Announcement authorised by the Board of Directors of Actinogen Medical

About Actinogen Medical

Actinogen Medical (ACW) is an ASX-listed, biotechnology company developing a novel therapy for neurological and neuropsychiatric diseases associated with dysregulated brain cortisol. There is a strong association between cortisol and detrimental changes in the brain, affecting cognitive function, harm to brain cells and long-term cognitive health.

Cognitive function means how a person understands, remembers and thinks clearly. Cognitive functions include memory, attention, reasoning, awareness and decision-making.

Actinogen is currently developing its lead compound, Xanamem, as a promising new therapy for Alzheimer's Disease and Depression and hopes to study Fragile X Syndrome and other neurological and psychiatric diseases in the future. Reducing cortisol inside brain cells could have a positive impact in these and many other diseases. The cognitive dysfunction, behavioural abnormalities, and neuropsychological burden associated with these conditions is debilitating for patients, and there is a substantial unmet medical need for new and improved treatments.

Current and Upcoming Clinical Trials

The **XanaCIDD Phase 2a depression trial** is a double-blind, six-week proof-of-concept, placebo-controlled, parallel group design trial in 160 patients. Patients are evenly randomized to receive Xanamem 10 mg once daily or placebo, in some cases in addition to their existing antidepressant therapy, and effects on cognition and depression are assessed.

The **XanaMIA Phase 2b Alzheimer's disease trial** is a double-blind, 36-week treatment, placebo-controlled, parallel group design trial in 220 patients with mild to moderate AD and progressive disease, determined by clinical criteria and confirmed by an elevated level of the pTau181 protein biomarker in blood. Patients receive Xanamem 10 mg or placebo, once daily, and effects on cognition, function and progression of Alzheimer's disease are assessed. Thus, Xanamem is being assessed in this trial for its potential effects as a both a cognitive enhancer and a disease course modifier.

About Xanamem

Xanamem's novel mechanism of action is to block the production of cortisol inside cells through the inhibition of the 11β-HSD1 enzyme in the brain. Xanamem is designed to get into the brain after it is absorbed in the intestines upon swallowing.

Chronically elevated cortisol is associated with cognitive decline in Alzheimer's Disease and excess cortisol is known to be toxic to brain cells. Cognitive impairment is also a feature in Depression and many other diseases. Cortisol itself is also associated with depressive symptoms and when targeted via other mechanisms has shown some promise in prior clinical trials.

The Company has studied 11β-HSD1 inhibition by Xanamem in more than 300 volunteers and patients, so far finding a statistically significant improvement in working memory and attention, compared with placebo, in healthy, older volunteers in two consecutive trials and clinically significant improvements in functional and cognitive ability in patients with biomarker-positive mild AD. Previously, high levels of target engagement in the brain with doses as low as 5 mg daily have been demonstrated in a human PET imaging study. A series of Phase 2 studies in multiple diseases is being conducted to further confirm and characterize Xanamem's therapeutic potential.

Xanamem is an investigational product and is not approved for use outside of a clinical trial by the FDA or by any global regulatory authority. Xanamem® is a trademark of Actinogen Medical.

Disclaimer

This announcement and attachments may contain certain "forward-looking statements" that are not historical facts; are based on subjective estimates, assumptions and qualifications; and relate to circumstances and events that have not taken place and may not take place. Such forward looking statements should be considered "at-risk statements" - not to be relied upon as they are subject to known and unknown risks, uncertainties and other factors (such as significant business, economic and competitive uncertainties / contingencies and regulatory and clinical development risks, future outcomes and uncertainties) that may lead to actual results being materially different from any forward looking statement or the performance expressed or implied by such forward looking statements. You are cautioned not to place undue reliance on these forward-looking statements that speak only as of the date hereof. Actinogen Medical does not undertake any obligation to revise such statements to reflect events or any change in circumstances arising after the date hereof, or to reflect the occurrence of or non-occurrence of any future events. Past performance is not a reliable indicator of future performance. Actinogen Medical does not make any guarantee, representation or warranty as to the likelihood of achievement or reasonableness of any forward-looking statements and there can be no assurance or guarantee that any forward-looking statements will be realised.

ACTINOGEN MEDICAL ENCOURAGES ALL CURRENT INVESTORS TO GO PAPERLESS BY REGISTERING THEIR DETAILS WITH THE DESIGNATED REGISTRY SERVICE PROVIDER, AUTOMIC GROUP.

Appendix 4C

Quarterly cash flow report for entities subject to Listing Rule 4.7B

Name of entity	
ACTINOGEN MEDICAL LIMITED	
ABN	**Quarter ended ("current quarter")**
14 086 778 476	31 December 2023

Consolidated statement of cash flows		**Current quarter $A'000**	**Year to date (6 months) $A'000**
1.	**Cash flows from operating activities**		
1.1	Receipts from customers		
1.2	Payments for		
	(a) research and development	(4,971)	(8,196)
	(b) product manufacturing and operating costs		
	(c) advertising and marketing		
	(d) leased assets		
	(e) staff costs	(888)	(2,274)
	(f) administration and corporate costs	(605)	(1,096)
1.3	Dividends received (see note 3)	-	-
1.4	Interest received	34	106
1.5	Interest and other costs of finance paid	(6)	(10)
	Income taxes paid	-	-
1.7	Government grants and tax incentives	4,793	4,793
1.8	Other (working capital movements)	14	123
1.9	**Net cash from / (used in) operating activities**	**(1,629)**	**(6,554)**

2.	**Cash flows from investing activities**		
2.1	Payments to acquire or for:		
	(a) entities		
	(b) businesses		
	(c) property, plant and equipment		
	(d) investments		
	(e) intellectual property		
	(f) other non-current assets		
2.2	Proceeds from disposal of:		
	(a) entities		
	(b) businesses		

Consolidated statement of cash flows		Current quarter $A'000	Year to date (6 months) $A'000
	(c) property, plant and equipment		
	(d) investments		
	(e) intellectual property		
	(f) other non-current assets		
2.3	Cash flows from loans to other entities		
2.4	Dividends received (see note 3)		
2.5	Other (provide details if material)		
2.6	**Net cash from / (used in) investing activities**	**-**	**-**

3.	**Cash flows from financing activities**		
3.1	Proceeds from issues of equity securities (excluding convertible debt securities)	-	10,001
3.2	Proceeds from issue of convertible debt securities		
3.3	Proceeds from exercise of options		
3.4	Transaction costs related to issues of equity securities or convertible debt securities	-	(454)
3.5	Proceeds from borrowings		
3.6	Repayment of loan shares by Managing Director		
3.7	Transaction costs related to loans and borrowings		
3.8	Dividends paid		
3.9	Other		
3.10	**Net cash from / (used in) financing activities**	**-**	**9,547**

4.	**Net increase / (decrease) in cash and cash equivalents for the period**		
4.1	Cash and cash equivalents at beginning of period	13,084	8,460
4.2	Net cash from / (used in) operating activities (item 1.9 above)	(1,629)	(6,554)
4.3	Net cash from / (used in) investing activities (item 2.6 above)	-	-
4.4	Net cash from / (used in) financing activities (item 3.10 above)	-	9,547
4.5	Effect of movement/adjustment in exchange rates on cash held	(1)	1
4.6	**Cash and cash equivalents at end of period**	**11,454**	**11,454**

5.	Reconciliation of cash and cash equivalents at the end of the quarter (as shown in the consolidated statement of cash flows) to the related items in the accounts	Current quarter $A'000	Previous quarter $A'000
5.1	Bank balances	2,454	10,084
5.2	Call deposits	9,000	3,000
5.3	Bank overdrafts		
5.4	Other – restricted cash re office lease		
5.5	**Cash and cash equivalents at end of quarter (should equal item 4.6 above)**	**11,454**	**13,084**

6.	Payments to related parties of the entity and their associates	Current quarter $A'000
6.1	Aggregate amount of payments to related parties and their associates included in item 1	195
6.2	Aggregate amount of payments to related parties and their associates included in item 2	-

Note: if any amounts are shown in items 6.1 or 6.2, your quarterly activity report must include a description of, and an explanation for, such payments.

Payments relate to salaries & fees paid to Directors of the Company during the quarter.

7.	Financing facilities *Note: the term "facility' includes all forms of financing arrangements available to the entity.* *Add notes as necessary for an understanding of the sources of finance available to the entity.*	Total facility amount at quarter end $A'000	Amount drawn at quarter end $A'000
7.1	Loan facilities		
7.2	Credit standby arrangements		
7.3	Other (please specify)		
7.4	**Total financing facilities**		
7.5	**Unused financing facilities available at quarter end**		
7.6	Include in the box below a description of each facility above, including the lender, interest rate, maturity date and whether it is secured or unsecured. If any additional financing facilities have been entered into or are proposed to be entered into after quarter end, include a note providing details of those facilities as well.		

8.	Estimated cash available for future operating activities	$A'000
8.1	Net cash from / (used in) operating activities (item 1.9)	(1,629)
8.2	Cash and cash equivalents at quarter end (item 4.6)	11,454
8.3	Unused finance facilities available at quarter end (item 7.5)	-
8.4	Total available funding (item 8.2 + item 8.3)	11,454
8.5	**Estimated quarters of funding available (item 8.4 divided by item 8.1)**	7.03

Note: if the entity has reported positive net operating cash flows in item 1.9, answer item 8.5 as "N/A". Otherwise, a figure for the estimated quarters of funding available must be included in item 8.5.

8.6 If item 8.5 is less than 2 quarters, please provide answers to the following questions:

8.6.1 Does the entity expect that it will continue to have the current level of net operating cash flows for the time being and, if not, why not?

Answer: N/A

8.6.2 Has the entity taken any steps, or does it propose to take any steps, to raise further cash to fund its operations and, if so, what are those steps and how likely does it believe that they will be successful?

Answer: N/A

8.6.3 Does the entity expect to be able to continue its operations and to meet its business objectives and, if so, on what basis?

Answer: N/A

Note: where item 8.5 is less than 2 quarters, all of questions 8.6.1, 8.6.2 and 8.6.3 above must be answered.

Compliance statement

1 This statement has been prepared in accordance with accounting standards and policies which comply with Listing Rule 19.11A.

2 This statement gives a true and fair view of the matters disclosed.

Date: 30 January 2024

Authorised by: By the Board
(Name of body or officer authorising release – see note 4)

Notes

1. This quarterly cash flow report and the accompanying activity report provide a basis for informing the market about the entity's activities for the past quarter, how they have been financed and the effect this has had on its cash position. An entity that wishes to disclose additional information over and above the minimum required under the Listing Rules is encouraged to do so.

2. If this quarterly cash flow report has been prepared in accordance with Australian Accounting Standards, the definitions in, and provisions of, *AASB 107: Statement of Cash Flows* apply to this report. If this quarterly cash flow report has been prepared in accordance with other accounting standards agreed by ASX pursuant to Listing Rule 19.11A, the corresponding equivalent standard applies to this report.

3. Dividends received may be classified either as cash flows from operating activities or cash flows from investing activities, depending on the accounting policy of the entity.

4. If this report has been authorised for release to the market by your board of directors, you can insert here: "By the board". If it has been authorised for release to the market by a committee of your board of directors, you can insert here: "By the [*name of board committee – eg Audit and Risk Committee*]". If it has been authorised for release to the market by a disclosure committee, you can insert here: "By the Disclosure Committee".

5. If this report has been authorised for release to the market by your board of directors and you wish to hold yourself out as complying with recommendation 4.2 of the ASX Corporate Governance Council's *Corporate Governance Principles and Recommendations*, the board should have received a declaration from its CEO and CFO that, in their opinion, the financial records of the entity have been properly maintained, that this report complies with the appropriate accounting standards and gives a true and fair view of the cash flows of the entity, and that their opinion has been formed on the basis of a sound system of risk management and internal control which is operating effectively.